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EXAMINER

SHARAREH, SHAHNAM J

ART UNIT PAPER NUMBER

1617

DATE MAILED: 09/23/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/763,236

Applicant(s)

FREEMAN ET AL.

Examiner

Shahnam Sharareh

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 24-50 is/are pending in the application.
- 4a) Of the above claim(s) 31 and 33-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 24-28, 32 and 37-50 is/are rejected.
- 7) ☒ Claim(s) 29 and 30 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 15.
- 4) ☐ Interview Summary (PTO-413) Paper No(s) _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

DETAILED ACTION

Amendment filed on July 18, 2003 has been entered. Claims 24-38, 40-50 are pending. Claims 31, 33-36 are withdrawn for the reasons of record.

1. Applicant's traversal for the election requirement is noted, but not persuasive for the reasons of record. Applicant's arguments have been addressed in previous response. Applicant argues that there exists no lack of unity. Applicant appears to be arguing that function of the elected all various species are the same as described in Scheme I of the specification. This is not found persuasive, because the invention is directed to a compound, not it's mode of action. Accordingly, the lack of novelty is assessed based on the compound itself, not its functionality.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. The prosecution of the claims is to the extent that claims read on the species of -NH as the linker, hydrogen as the R1-R3, and alkyl as the R4. Accordingly, claim 29-30 are free of art with respect to the elected species.

Any rejection that is not addressed in this Office Action is considered obviated in view of the Amendments.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 24-28, 37-48 are rejected under 35 U.S.C. 102(a) as being anticipated by Rauth et al (Int. J. Radiation Oncology boil Phys. Vol 42 No. 4 pp. 755-762 1998).

Applicant's arguments with respect to this rejection have been fully considered but are not persuasive. Applicant argues that Rauth does not disclose the compound of claim 24, because the compounds of Rauth do not teach the therapeutic agent to be released by virtue of a through bond elimination (see Response at page 13). Applicant appears to be arguing that the function provided by the instant compound is not taught by the cited references. In essence, Applicant appears to be arguing that the functionality of the instant compounds is the point of novelty.

In response, Examiner states that the instant claims are directed to conjugate compounds, which are drafted as "product by process" claims. Accordingly, products by process claims are not limited to the manipulations of the recited steps, only the structure implied by the steps (see MPEP 2113). Here, the claimed compounds require the following elements: (a) a bioreductive moiety, containing an aromatic ring substituted with a nitro group, with at least one therapeutic agent linked thereto, and (b) a physiologically acceptable derivatives thereof.

Further Applicant's attempt to narrow the scope of the claims by incorporating subject matter from the specification into the claim is improper. During prosecution, the claims are examined as presented. Here, the rejected claims are not directed to any particular formula or chemical structure. Rather, the instant claims are directed to compositions having structural and functional elements. Accordingly, since the cited prior art teach each descriptive element of the claims, it also anticipates the functional characteristics of the instant claims.

Rauth meets the structural limitations of the instant compound, namely, an aromatic reductive moiety linked to a therapeutic moiety. Thus its compounds inherently provide all functions associated with the instant claims. The bioactive active drug includes nitroimidazoleds, mitomycins and benzotriazine di N-oxides. Rauth describes the models for reduction process (see abstract, page 756-757). Compounds of Rauth are prepared in suitable physiological solutions thus they exist in with their suitable salts thereof. Rauth's Figure 8 shows various moieties with acridine-based nitro compounds that fall within the scope of the instant claims. Thus, claims stand rejected.

3. Claims 24-28, 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Hay et al (Anti-Cancer Drug Design 1996, IL 383-402).

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive. Applicant argues that the release of the therapeutic agent in Hay occurs via a "through space attack." In response, Examiner relies on the same argument set forth above for Rauth. First, the products by process claims are not limited to the features of the process, rather the limitations of the product. Second, Applicant's reliance on Scheme I of the instant specification to narrow the limitation of the instant claims is improper. Third, the instant claims do not exclude the compounds of Hays.

Hays meets all limitation of the instant products because it discloses nitroimidazol alkanoic acids wherein the compound is a bioconjugate comprising an aromatic bio-reductive moiety with a nitro group and an active drug, (compounds 4 of

Art Unit: 1617

Scheme 1, also page 397, Scheme 2, step v). Therefore, contrary to Applicant's arguments, all elements of the instant claim 24 is met.

4. Claims 24-28, 37-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Adams et al US Patent 5,652,255.

Applicant's arguments with respect to this rejection have been fully considered but are not found persuasive. Applicant argues that there exists no "releasable therapeutic drug." Applicant also argues that the therapeutic agent is does not undergo a "through bond elimination reaction." (see Response at page 16).

In reply, Examiner restates the same principles as argued in previous rejections. Thus, Adams nitric oxide synthase inhibitors meet the limitations of the instant claims (see col 10, 2nd col, col 14, lines 13-46, col 16, lines 33-60, col 19-20, examples 1-3). Adams is anticipatory to the instant claims.

Information Disclosure Statement

5. The information disclosure statement (IDS) filed July 25, 2003 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. The instant IDS did not contain a legible copy of the article by Jaffar et al titled "Bioreductive drugs: Selectivity towards hypoxic tissues,"

Expert Opinion on Therapeutic Patents 1999. Accordingly, this publication has not been considered.

Claim Objections

6. Claims 29-30 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims to the extent it has been examined.

Conclusion

No claims are allowed. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Art Unit: 1617

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

SS



RUSSELL TRAVERS
PRIMARY EXAMINER